

Survival Analysis with Cox Proportional Hazard Model for Tuberculosis (TBC) Patients

Zahratun Nisa, Bobby Poerwanto, Muhammad Fahmuddin Sudding

Universitas Negeri Makassar, Makassar, Indonesia

Article Info

Article history:

Received : 05-22-2023

Revised : 09-20-2023

Accepted : 10-20-2023

Keywords:

Cox Proportional Hazard;
Hazard Ratio;
Survival Analysis;
Tuberculosis.

ABSTRACT

Survival analysis is a method in statistics which aims to analyze the relationship between time from the beginning of observation until the occurrence of an event (response variable) with factors that have an influence on the event (predictor variables). To determine the relationship between the response variable and the predictor variable, where the response variable is the time until the event occurs, one method that can be used is the cox proportional hazard regression method. The data used in this research is data on hospitalizations of tuberculosis sufferers at Haji Makassar Hospital in 2022 because it has characteristics that are in accordance with the aim of survival analysis, namely to determine the relationship between the life span of TBC patients and the factors that influence TBC disease. The results of the analysis obtained factors that significantly influence the recovery rate of patients with TBC are shortness of breath and smoking habits. The shortness of breath variable has an influence on the recovery rate of TBC patients, namely 0,3506, which means that TBC patients who do not experiencing shortness of breath has a recovery rate of 0.3506 times the likelihood of recovery compared to patients who experience shortness of breath. Variable smoking habit was 0.7367, which means that patients with TBC did not smoking habit has a recovery rate of 0.7367 times recovered compared to patients who had a smoking habit.



Accredited by Kemenristekdikti, Decree No: 200/M/KPT/2020

DOI: <https://doi.org/10.30812/varian.v7i1.2994>

Corresponding Author:

Bobby Poerwanto,
Department of Statistics, Universitas Negeri Makassar.
Email: bobby_poerwanto@unm.ac.id

Copyright ©2023 The Authors.

This is an open access article under the [CC BY-SA](https://creativecommons.org/licenses/by-sa/4.0/) license.



How to Cite:

Nisa, Z., Poerwanto, B., & Fahmudin, M., (2023). Survival Analysis with Cox Proportional Hazard Model for Tuberculosis (TBC) Patients. *Jurnal Varian*, 7(1), 77-86.

This is an open access article under the CC BY-SA license (<https://creativecommons.org/licenses/by-sa/4.0/>)

A. INTRODUCTION

Survival analysis is a method in statistics that is used to analyze data from the response variable, namely the time the observation starts until an event occurs. Event are a special occurrence that can occur in an individual, such as healing, recurrence of another disease, or death. The time of an event can be expressed in years, months, weeks, or days (Fernandes et al., 2016). The purpose of the survival analysis is to determine the relationship between the time of occurrence (response variable) and the predictor variable at the time of the study. In addition, it is also used to see what factors have a significant influence on an event (Annas et al., 2018) (Poerwanto et al., 2018). The characteristic of survival data is that it often cannot be observed completely, it is called censored data. This is due to the limitations of the observations made or the individuals observed leaving the study (Turkson et al., 2021).

Finding the relationship between the response variable and the predictor variable can be done using the regression analysis method (Dewi et al., 2020; Bustan and Poerwanto, 2021). Several regression models that can be used in survival analysis include parametric models, nonparametric models, and semiparametric models. Of the three models, there is a semiparametric model that has better model flexibility because some of the variables follow a common distribution. In addition, the semiparametric model is a safe model to choose when you are in doubt about determining the parametric model and the estimator results are almost the same as the estimator results with the parametric model (Chandra and Rohmaniah, 2019).

The cox regression model is a semiparametric regression model and fulfills the proportional hazard assumption, so it is commonly known as the cox proportional hazard regression model ((Dukalang, 2019); (Fa'rifah and Poerwanto, 2019)). This method can estimate the hazard ratio used to compare hazard values in a group of individuals with other groups of individuals to fulfill the proportional hazard assumption. This method can also estimate the regression parameters well even though the basic hazard is unknown (Fernandes et al., 2016).

Analysis survival is an analysis that has received attention in the health and medical fields that can be used to analyze the patient's survival time against a disease (Faisal et al., 2020). In this study, the data used were TBC patient data at Haji Makassar Hospital in 2022. Tuberculosis is an infectious disease caused by the Mycobacterium Tuberculosis bacterium. The germs are transmitted from TBC sufferers who talk, sneeze, or cough, splashing phlegm through the air. Nearly a quarter of the world's population is infected with Mycobacterium Tuberculosis, about 89% of TBC affects adults, and 11% affects children. Tuberculosis (TBC) is currently still a public health problem both in Indonesia and internationally so that it becomes one of the goals of sustainable health development (SDGs). Until now TBC is still the highest cause of death after HIV/AIDS and is one of the 20 main causes of death worldwide (Ministry of Health of the Republic of Indonesia, 2022).

According to WHO in the 2021 Global Tuberculosis Report, globally it is estimated that 9.9 million people will suffer from TBC in 2020. The number of deaths from tuberculosis globally in 2020 is 1.3 million, when compared to 2019 which is 1.2 million. these cases have increased. in 2020 the number of TBC cases in Indonesia will be 301 per 100,000 population. India has the third highest TBC case rate in the world after India and China (Ministry of Health of the Republic of Indonesia, 2022).. Specifically for South Sulawesi Province in 2020, the number of TBC sufferers per Regency/City was 18,863 cases, with details of 11,095 men and 7,768 women. Makassar City is the city with the highest TBC cases in South Sulawesi Province with 5,421 sufferers, followed by Gowa District with 1,810 sufferers (South Sulawesi Health Service, 2021).

Survival analysis using the Cox proportional hazards regression model has been carried out by several researchers to analyze the rate of recovery of patients from a disease. A comparison of the Cox regression model and the Fine and Gray model to determine the risk factors that influence the survival of arthroplasty patients was carried out by (Ranstam and Robertsson, 2017). The results of research using Cox regression analysis provide better results than analysis using Fine and Gray, because parameter estimates from the Fine and Gray model can be misleading if interpreted in terms of relative risk. One study that used the Cox proportional hazard regression method was conducted by Royston and Altman (2013). The result of the research is that the survival of a patient from a disease is related to survival data so that survival analysis and Cox regression can be used, namely a mathematical model approach to describe the survival curve by considering several risk factors simultaneously.

Based on the background description above, the purpose of this study is to identify factors that influence the cure rate for TBC sufferers at Haji Makassar Hospital using survival analysis with the Cox proportional hazard regression method, The hope is to be able to sign an increasing number of cases.

B. RESEARCH METHOD

1. Data Source

The data used in this study is secondary data and to bring together the variables used in this study, namely the factors that affect the recovery rate of TBC patients at Haji Makassar Hospital in 2022. After data collection, the number of TBC patients at Haji Makassar Hospital was obtained from January to December 2022 with a total of 184 patients. Of the 184 patients data, after testing the existing assumptions in the cox proportional hazard regression method, it turned out that only 170 TBC patients data met the assumptions. So that out of the 184 total population of TBC patients at Haji Makassar Hospital in 2022, 170 samples met the assumptions.

2. Variable Operational Definition

Table 1. Variable Operational Definition

Variable	Variable Name	Descriptive
Y	Survival Time	The length of time a TBC patient has been treated (inpatient and/or outpatient) at the hospital (Days).
S	Status	0 = Failure (absent/died during observation); 1 = Success (healed)
X_1	Age	Age at diagnosis of TBC disease (Years)
X_2	Gender	0 = Female; 1 = Male
X_3	Cough with Phlegm	0 = Not coughing up phlegm; 1 = Cough with phlegm
X_4	Hard to Breathe	0 = Not hard to breathe; 1 = Hard to breathe
X_5	Night Sweat	0 = Not night sweats; 1 = Night sweat
X_6	Smoking Habit	0 = Not smoke; 1 = Smoke
X_7	History Status	0 = New case; 1 = Relapse case
X_8	Drug Status	0 = Not take medicine regularly; 1 = Take medicine regularly

3. Research Procedure

The research procedure carried out is given in Figure 1.

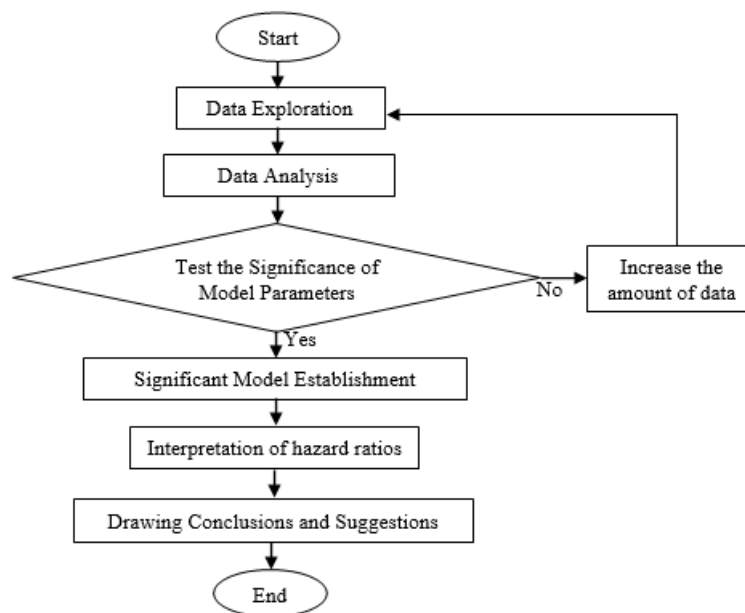


Figure 1. Research Procedure Flowchart Diagram

4. Data Analysis Technique

1. Data Exploration.

At this stage, researchers prepare patient survival time data, namely determining the starting point, end point, and time measurement scale in the study. The starting point in this study was the admission of TBC patients to the hospital, while the end point was determining the event status. The time measurement scale used in this research is days. In this study, right censoring was used with the observed event being healing.

2. Descriptive analysis of predictor variables and response variables.

3. Test the survival time distribution using the Kolmogorov Smirnov test (Chandra and Rohmaniah, 2019).

$$D = \max |F_n(x) - F_0(x)|$$

where

D : Kolmogorov-Smirnov method test statistics

$F_n(x)$: Hypothesized distribution function

$F_0(x)$: Empirical data distribution function.

4. Testing the proportional hazard assumption using the GOF test.

The Goodness of Fit (GOF) estimation method uses Schoenfeld residual test statistics to test the proportional hazard assumption as follows (Istuti et al., 2019):

$$z = \frac{r}{\frac{1}{\sqrt{n-1}}}$$

where

$$r = \frac{\sum_{j=1}^m (R_{ij} - \bar{R}_{ij})(RT_i - \bar{RT}_i)}{\sqrt{\sum_{j=1}^m (R_{ij} - \bar{R}_{ij})^2} \sqrt{\bar{R}_{ij}(RT_i - \bar{RT}_i)^2}}$$

$$R_{ij} = \delta_i \left(x_{ij} - \frac{\sum_{l \in R(t_i)} x_{il} \exp(\beta \hat{x}_l)}{\sum_{l \in R(t_i)} \exp(\beta \hat{x}_l)} \right)$$

where:

- z : Schoenfeld residual statistics test
- n : Number of data sampel
- r : Ranking survival time
- m : Number of i -th individuals
- R_{ij} : Schoenfeld residual of the j -th independent variable from the individual who experienced the event at time t_i
- \bar{R}_{ij} : Average schoenfeld residual of the j -th independent variable from the individual who experienced the event at time t_i
- RT_i : Ranking of survival time for the i -th individuals
- \bar{RT}_i : Average survival time ranking for the i -th individuals
- δ_i : Censorship indicator
- $\hat{\beta}$: Likelihood maximum estimator of β
- x_{ij} : Value of the j -th independent variable from the individual who experienced the event at time t_i

5. Parameter estimation for the cox proportional hazard regression estimator model using the maximum partial likelihood estimation (MLE) method is used as follows (Pertiwi and Purnami, 2020):

$$L(\beta) = \prod_{i=1}^r \left[\frac{\exp(\beta' x_i)}{\sum_{l \in R(t_i)} \exp(\beta' x_l)} \right]$$

where:

- $L(\beta)$: Maximum likelihood estimation of parameter β using the exact likelihood method
- r : Individuals who experience a success event
- β : Regression Coefficient
- x_i : Variable vector of individuals who failed at time- i
- x_l : Vector of individuals variable that are still alive and are elements of R_{t_i}
- R_{t_i} : The set of individuals who survived at time $-i$

After obtaining the likelihood function, it is then transformed into ln form and equalizes zero in the first derivative of the function. In estimating the β parameter, the Newton Raphson method is used to maximize the partial likelihood function.

6. Testing the significance of the parameters of the cox proportional hazard regression estimator model using simultaneous test and partial test (Fajarini and Fatekurohman, 2018).

(a) Simultaneous Test

$$G^2 = -2(\ln L_R - \ln L_F)$$

L_R : The value of the likelihood function in the model without variables

L_F : The value of the likelihood function in the model with variables.

(b) Partial Test

$$W^2 = \left[\frac{\hat{\beta}_h}{SE(\hat{\beta}_h)} \right]$$

$\hat{\beta}_h$: Parameter estimation of the h -th predictor variable

$SE(\hat{\beta}_h)$: Standard error of parameter estimates of the h -th predictor variable.

7. Formation of the final cox proportional hazard regression model with significant variables
8. Interpretation of the results of the hazard ratio from the cox proportional hazard regression model is suitable.
9. The conclusion of the entire data analysis that has been processed.

C. RESULTS AND DISCUSSION

1. Descriptive Analysis

The study with survival analysis involved 170 samples from 184 population of TBC patients at Haji Makassar Hospital in 2022, where 13 patients received treatment as short as 1 day and as long as 19 days as 1 patient and the average treatment was 7 days and status The event sensor observed successful events as many as 141 people (83%). The average age of TBC patients is 47 years, with the highest age being 84 years and the lowest age being 17 years. Then TBC disease is experienced by the majority of patients who are male (65%) so that the factor of smoking habits (59%) also occurs more frequently. For symptoms or conditions coughing up blood (55%), shortness of breath (97%), and night sweats (72%) mostly experienced by TBC sufferers. Patients with new history status (6%) experienced the majority of TBC patients, as well as regular treatment status (83%) experienced more TBC patients.

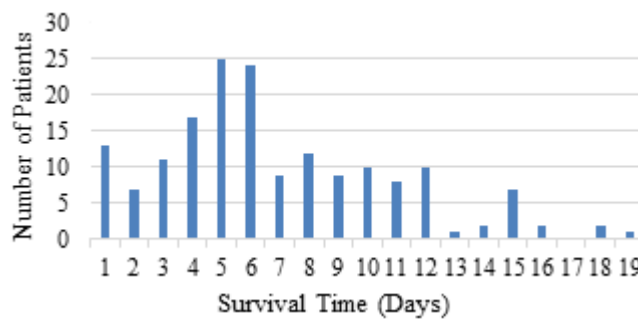


Figure 2. Survival Time Histogram

Table 2. Age of TBC Patients

Variable	Average (Year)	Maximum (Year)	Minimum (Year)
Age	47	84	17

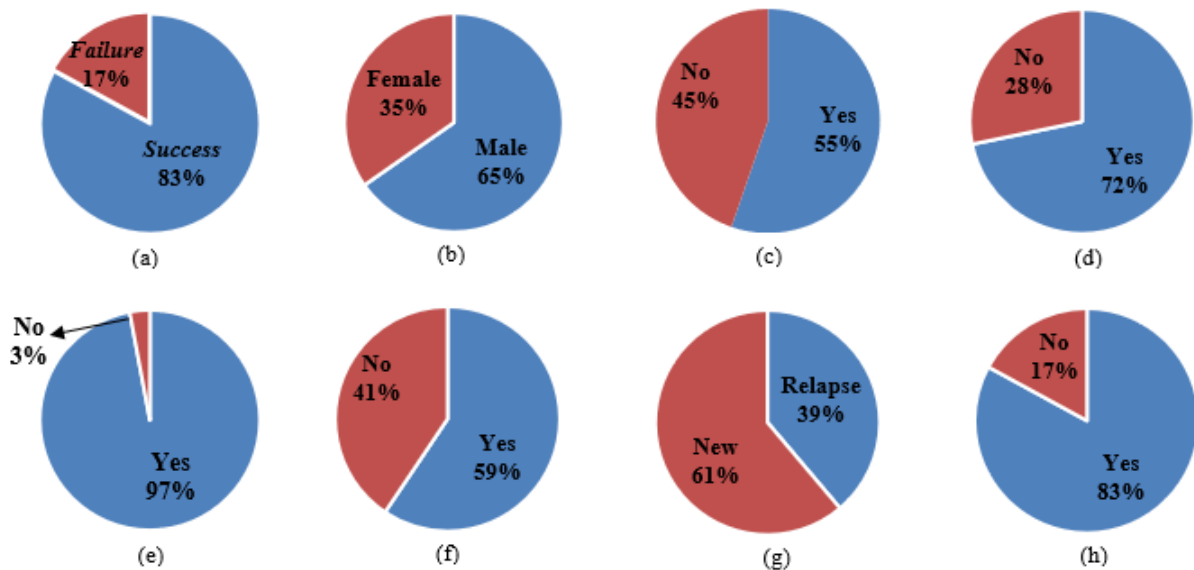


Figure 3. Pie Chart for (a) Event Censorship Status, (b) Gender, (c) Cough with Phlegm, (d) Night Sweat, (e) Hard to Breathe, (f) Smoking Habit, (g) History Status, (h) Drug Status

2. Survival Time Distribution Test

Distribution testing in this study was used to determine the distribution of the survival time data used, with the hypothesis being tested:

H_0 = Data meet the distribution tested.

H_1 = Data does not meet the distribution tested.

Table 3. Survival Time Distribution Test

Jenis Distribusi	P-Value	Information
Weibull	0,0473	Reject H_0
Gamma	0,0442	Reject H_0
Log Normal	0,0009	Reject H_0
Ekspensial	0,0000	Reject H_0

From Table 3, it can be seen that each distribution tested has a p-value < 0.05 , so it can be concluded that the decision to reject H_0 means that the survival time data does not meet distribution. As previously explained, Cox proportional hazards regression is a semiparametric model that does not require special information about the distribution underlying the survival time, so testing can be continued using the Cox proportional hazards regression method.

3. Proportional Hazard Assumption Testing

The proportional hazard assumption is said to be fulfilled if the p-value is > 0.05 significance level with the hypothesis being tested:

H_0 = Data meet the proportional hazard assumption.

H_1 = Data does not meet the proportional hazard assumption.

Table 4. Proportional Hazard Assumption Testing

Variabel	Coefficient	P-Value	Information
Age (X_1)	0,0152	0,9000	Accept H_0
Gender (X_2)	13,800	0,2400	Accept H_0
Cough with phlegm (X_3)	21,400	0,1400	Accept H_0
Hard to breathe (X_4)	0,1830	0,6700	Accept H_0
Night Sweat (X_5)	10,200	0,3100	Accept H_0
Smoking habit (X_6)	21,000	0,1500	Accept H_0
History Status (X_7)	0,1480	0,7000	Accept H_0
Drug Status (X_8)	0,0000	10,000	Accept H_0

Based on Table 4, it can be seen that each variable has a p-value > 0.05 , so it can be concluded that the decision to accept H_0 means that these variables meet the proportional hazard assumption or in other words the variables used have a proportional hazard value or risk effect between one individual and another and is constant over time so that the results will be easy to interpret.

4. Parameter Estimation of the Cox Proportional Hazard Regression Estimator Model

Table 5. Parameter Estimation of the Cox Proportional Hazard Regression Estimator Model

Variabel	Coefficient	P-Value	Information
Age (X_1)	0,0104	0,0701	Not Significant
Gender (X_2)	0,3070	0,1576	Not Significant
Cough with phlegm (X_3)	-0,2657	0,1617	Not Significant
Hard to breathe (X_4)	-0,9743	0,0377	Significant
Night Sweat (X_5)	0,2433	0,2211	Not Significant
Smoking habit (X_6)	-0,4518	0,0410	Significant
History Status (X_7)	-0,4736	0,8065	Not Significant
Drug Status (X_8)	17,280	0,9949	Not Significant

5. Parameter Significance Test

1. Simultaneous Test

The testing criteria in the simultaneous test are p-value < 0.05 significance level with the hypothesis being tested:

$H_0 : \beta_1 = \beta_2 = \dots = \beta_h = 0$ (none of the predictor variables were significant)

$H_1 : \beta_h \neq 0$, with $h = 1, 2, \dots, p$ (there is at least one significant predictor variable).

Based on Table 5, it can be seen that the p-value likelihood ratio is $0.0026 < 0.05$, so it can be concluded that the decision to reject H_0 means that there is at least one predictor variable that has a significant effect on the response variable in the model.

2. Partial Test

The testing criteria in the partial test are p-value < 0.05 significance level with the hypothesis being tested:

$H_0 : \beta_h = 0$, with $h = 1, 2, \dots, p$ (h predictor variable is not significant)

$H_1 : \beta_h \neq 0$ (h predictor variable is significant).

Based on Table 5, it can be seen that the predictor variables for shortness of breath and smoking habits have a p-value < 0.05 , so it can be concluded that the decision to reject H_0 means that the two predictor variables have a significant effect on the recovery rate of TBC patients at Haji Makassar Hospital.

6. Final Cox Proportional Hazard Regression Model with Significant Variables

Table 6. Final Cox Proportional Hazard Regression Model with Significant Variables

Variable	Coefficient	Hazard Ratio	P-Value
Hard to breathe (X_4)	-10,480	0,3506	0,0229
Smoking habit (X_6)	- 0,3056	0,7367	0,0760
Likelihood Ratio			0,0340

Based on the parameter estimation results in Table 6, the final cox proportional hazard regression model is obtained as follows:

$$h(t) = h_0(t) \exp(-1,0480X_4 - 0,3056X_6)$$

From the cox proportional hazard model with significant variables, another simultaneous test was carried out to find out whether the model was truly significant or not. Based on Table 6, it can be seen that the p-value likelihood ratio is $0.0340 < 0.05$, so it can be concluded that the decision to reject H_0 means that at least there is one predictor variable that is significant so that the cox proportional hazard model is significant.

7. Hazard Ratio Significant Variable

Based on Table 6, it can be seen that the hazard ratio value for the shortness of breath variable is 0.3506 and the smoking habit variable is 0.7367. A hazard ratio value of less than 1 indicates a preventive factor or has a smaller risk of failure (Chandra and Rohmaniah, 2019). So that TBC patients who do not experience shortness of breath have a recovery rate of 0.3506 times more likely to recover than those who experience shortness of breath, likewise those who do not smoke have a recovery rate of 0.7367 times more likely to recover than those who smoke.

This study is directly proportional to research conducted by Tamara et al. (2021), which was published in a medical journal where shortness of breath and smoking habits have an influence on TBC disease. TBC patients have many various complaints that can cause breathing problems, one of which can cause shortness of breath due to airway obstruction caused by TBC germs. Shortness of breath occurs in advanced TBC disease, where the infiltration has covered half of the lungs. Smoking habits increase the risk of suffering from TBC because the toxic content such as tar inhaled from cigarette smoke can interfere with the clarity of the ciliary mucosa which is used as the main defense mechanism in causing changes in the structure and function of the airways and lung tissue, as well as the host's immunological response to infection.

D. CONCLUSION AND SUGGESTION

Based on the results of research and discussions that have been carried out on TBC patient data at Haji Makassar Hospital in 2022, it can be concluded that to obtain the final model, namely estimating the parameters and testing the significance of the parameters of

the variables used and then obtaining significant variables and eliminating variables. which is not significant. Then the parameter estimation is carried out again and the significance of the parameters is tested only on previously significant variables. So you will get the final cox proportional hazards regression model with significant variables, as follows:

$$h(t) = h_0(t)\exp(-1,0480X_4 - 0,3056X_6)$$

It can be seen in the model above that there are two significant variables, namely X_4 (shortness of breath) and X_6 (smoking habit). The shortness of breath variable has an influence on the cure rate for TBC patients, namely $e^{-1,0480} = 0,3506$ and the smoking habit variable $e^{-0,3056} = 0,7367$. A hazard ratio value of less than 1 indicates a preventive factor or has a smaller risk of failure. So that TBC patients who do not experience shortness of breath have a recovery rate of 0.3506 times more likely to recover than those who experience shortness of breath, likewise those who do not smoke have a recovery rate of 0.7367 times more likely to recover than those who smoke.

For further research, to prioritize complete data to reduce censored data and it is necessary to add predictor variables related to the social and environmental conditions of patients suffering from Tuberculosis, because the social conditions of sufferers are also considered to influence the success rate of treatment of Tuberculosis patients, such as knowledge related to TB, home and environmental conditions. around, and so on. For people who have a smoking habit and experience shortness of breath, they should immediately see a doctor to avoid TBC disease, and if they have been infected, they should take regular treatment and avoid things that can make TBC disease worse.

DECLARATIONS

AUTHOR CONTRIBUTION

All authors contributed to the writing of this article.

FUNDING STATEMENT

-

COMPETING INTEREST

The authors declare no conflict of interest in this article.

REFERENCES

- Annas, S., Nusrang, M., Arisandi, R., Fadillah, N., and Kartikasari, P. (2018). Cox proportional hazard regression analysis of dengue hemorrhagic fever. In *Journal of Physics: Conference Series*, volume 1028, page 012242. IOP Publishing. DOI : <https://doi.org/doi:10.1088/1742-6596/1028/1/012242>.
- Bustan, M. and Poerwanto, B. (2021). Logistic regression model of relationship between breast cancer pathology diagnosis with metastasis. In *Journal of Physics: Conference Series*, volume 1752, page 012026. IOP Publishing. DOI : <https://doi.org/10.1088/1742-6596/1752/1/012026>.
- Chandra, N. E. and Rohmaniah, S. A. (2019). Analisis survival model regresi semiparametrik pada lama studi mahasiswa. *Jurnal Ilmiah Teknosains*, 5(2):94–98.
- Dewi, A. Y., Dwidayati, N. K., and Agoestanto, A. (2020). Analisis survival model regresi cox dengan metode mle untuk penderita diabetes mellitus. *Unnes Journal Of Mathematics*, 9(1):31–40.
- Dukalang, H. H. (2019). Analisis regresi cox proportional hazard pada pemodelan waktu tunggu mendapatkan pekerjaan. *Jambura Journal of Mathematics*, 1(1):36–42.
- Faisal, A. R., Bustan, M. N., and Annas, S. (2020). *Analisis Survival Dengan Pemodelan Regresi Cox Proportional Hazard Menggunakan Pendekatan Bayesian (Studi Kasus: Pasien Rawat Inap Penderita Demam Tifoid Di Rsud Haji Makassar)*. PhD thesis, UNIVERSITAS NEGERI MAKASSAR.
- Fajarini, F. A. and Fatekurohman, M. (2018). Analisis premi asuransi jiwa menggunakan model cox proportional hazard. *Indonesian Journal of Applied Statistics*, 1(2):88–99.

- Fa'rifah, R. Y. and Poerwanto, B. (2019). Platelets and hematocrit in the survival model of dengue hemorrhagic fever (dhf) sufferers in palopo. In *Materials Science Forum*, volume 967, pages 3–8. Trans Tech Publ.
- Fernandes, A. A. R. et al. (2016). *Pemodelan Statistika Pada Analisis Reliabilitas Dan Survival*. Universitas Brawijaya Press.
- Istuti, D. M. et al. (2019). Analisis ketahanan hidup data ties pasien tuberkulosis dengan metode exact likelihood pada model regresi cox proportional hazard. *MATHunesa: Jurnal Ilmiah Matematika*, 7(2).
- Ministry of Health of the Republic of Indonesia (2022). *Indonesia Health Profile 2021*. Jakarta: Ministry of Health of the Republic of Indonesia.
- Pertiwi, I. N. and Purnami, S. W. (2020). Regresi cox proportional hazard untuk analisis survival pasien kanker otak di c-tech labs edwar technology tangerang. *Inferensi*, 3(2):65–72.
- Poerwanto, B., Fa'Rifah, R., Sanusi, W., and Side, S. (2018). A matlab code to compute prediction of survival trends in patients with dhf. In *Journal of Physics: Conference Series*, volume 1028, page 012113. IOP Publishing. DOI : <https://doi.org/10.1088/1742-6596/1028/1/012113>.
- Ranstam, J. and Robertsson, O. (2017). The cox model is better than the fine and gray model when estimating relative revision risks from arthroplasty register data. *Acta orthopaedica*, 88(6):578–580. DOI : <https://doi.org/10.1080/17453674.2017.1361130>.
- Royston, P. and Altman, D. G. (2013). External validation of a cox prognostic model: principles and methods. *BMC medical research methodology*, 13:1–15. DOI : <https://doi.org/10.1186/1471-2288-13-33>.
- South Sulawesi Health Service (2021). *South Sulawesi Province Health Profile 2021*. Makassar: South Sulawesi Province Health Profile 2021.
- Tamara, D. V., Nurhayati, S., and Ludiana, L. (2021). Penerapan inhalasi sederhana menggunakan aromaterapi daun mint (mentha piperita) terhadap sesak nafas pada pasien tb paru. *Jurnal Cendikia Muda*, 2(1):40–49.
- Turkson, A. J., Ayiah-Mensah, F., and Nimoh, V. (2021). Handling censoring and censored data in survival analysis: a standalone systematic literature review. *International journal of mathematics and mathematical sciences*, 2021:1–16. DOI : <https://doi.org/10.1155/2021/9307475>.

[This page intentionally left blank.]